
Branched-chain amino acid depletion conditions bone marrow for hematopoietic stem cell transplantation avoiding amino acid imbalance-associated toxicity.

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Public Summary:

Blood or hematopoietic stem cells (HSCs) are used clinically in bone marrow (BM) transplantation due to their unique ability to reform the entire hematopoietic system. Recently, we reported that HSCs are highly sensitive to the amino acid valine, one of the three branched-chain amino acids (BCAAs) in addition to the amino acids isoleucine and leucine. Dietary depletion of valine could even be used as a conditioning regimen for HSC transplantation. Here, we report that depletion of all three BCAAs was significantly less toxic to mice than depletion of valine only, providing evidence that BCAA depletion may be a safer strategy to deplete HSCs in vivo.

Scientific Abstract:

Hematopoietic stem cells (HSCs) are used clinically in bone marrow (BM) transplantation due to their unique ability to reform the entire hematopoietic system. Recently, we reported that HSCs are highly sensitive to valine, one of the three branched-chain amino acids (BCAAs) in addition to isoleucine and leucine. Dietary depletion of valine could even be used as a conditioning regimen for HSC transplantation. Here, we report that HSCs are highly sensitive to the balance of BCAAs, with both proliferation and survival reduced by BCAA imbalance. However, low but balanced BCAA levels failed to rescue HSC maintenance. Importantly, in vivo depletion of all three BCAAs was significantly less toxic than depletion of valine only. We demonstrate that BCAA depletion can replace valine depletion as a safer alternative to BM conditioning. In summary, by determining HSC metabolic requirements, we can improve metabolic approaches to BM conditioning.

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